

Table 1 Frequencies of HLA Class I Alleles That are Known to Serve as HIV CTL Restriction Elements in Four Populations

HLA Alleles	Frequencies*			
	African Americans	USA Caucasians	North American Indians	Thais
A2	16.7	28.3	25.5	25.5
A3	8.9	12.2	2.9	1.5
A11	2.3	5.5	1.0	32.5
A24	4.7	9.6	19.6	14.6
A28	10.9	4.5	6.9	0.8
A30	9.5	2.6	2.0	1.1
A31	1.7	2.0	27.5	1.7
A32	1.0	5.1	2.0	0.2
A33	8.1	1.0	1.0	13.6
B7	8.3	10.0	3.9	2.7
B8	3.2	10.0	5.6	0.2
B12 (44)	6.2	10.4	3.9	5.4
B13	0.9	3.0	1.0	9.3
B14	3.0	4.1	2.9	0.4
B17	10.9	4.9	1.0	8.1
B18	3.3	4.9	1.0	2.5
B27	1.6	4.1	2.9	6.0
B35	7.7	8.5	18.6	2.5
B37	0.9	2.2	0.0	1.4
B52	1.1	1.2	2.9	3.1
B53	12.8	0.8	0.0	0.0
B57	4.2	3.9	1.0	5.2
B60	1.3	4.5	2.9	8.3
B62	1.4	5.5	4.9	5.0
Cw3	9.6	12.6	22.4	15
Cw4	21.0	9.8	15.4	6

*Frequencies for HLA-A and HLA-B alleles are taken from HLA 1991 [21], HLA-C for African Americans and USA Caucasians are taken from Histocompatibility Testing 1984 [19], HLA-C for North American Indians from Williams and McAuley, 1992 [22], and HLA-C for Thais from the Proceedings of the Second Asia and Oceania Histocompatibility Workshop Conference [23].

Table 2 Proportion of each of the four populations that would be predicted to present peptides to the immune system

Population	HLA Restriction Elements Chosen	HTV Protein	Epitope Location	Epitope
a) African Americans	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A28, B14	gp41	583-592	VERVYKDDQQL
	A30, B8	gp41	844-863	RRIRQGLERALL
	B17, B37	nef	117-128	TQGYFPQWQNYT
	Cw4	gp120	576-583	(S) FNCGGEFF
<i>(Proportion of African Americans expected to present these 5 epitopes is 92.3%)</i>				
b) USA Caucasians	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A30, B8	gp41	844-863	RRIRQGLERALL
	B7	gp120	302-312*	RFNNNTRKSI
		nef	126-138*	NYTPGPGVRYPLT
	B12	p24	169-184	IPMFSALESEGATPQDL
<i>(Proportion of USA Caucasians expected to present these 4 epitopes is 90.2%)</i>				
c) North American Indians	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFCGWCYK
	A31	gp41	770-780	RLRDLLLIVTR
<i>(Proportion of North American Indians expected to present these 3 epitopes is 96.4%)</i>				
d) Thais	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFCGWCYK
<i>(Proportion of Thais expected to present these 2 epitopes is 93.6%)</i>				
e) African Americans USA Caucasians North American Indians Thais	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A28, B14	gp41	583-592	VERVYKDDQQL
	A30, B8	gp41	844-863	RRIRQGLERALL
	B17, B37	nef	117-128	TQGYFPQWQNYT
	Cw4	gp120	376-383	(S) FNCGGEFF
	B7	gp120	302-312*	RFNNNTRKSI
		nef	126-138*	NYTPGPGVRYPLT
	B12	p24	169-184	IPMFSALESEGATPQDL
	A31	gp41	770-780	RLRDLLLIVTR
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFCGWCYK
<i>(Proportions of African Americans, USA Caucasians, North American Indians, and Thais expected to present these 9 epitopes are 95.4%, 97.5%, 99.4%, and 97.2%, respectively)</i>				

*The criteria upon which choices among peptides should be made are not yet known. It may be important to choose peptides that have been reported to be immunogenic in non-progressors to AIDS or that have been reported to induce immunodominant anti-HTV T-cell responses.

TABLE 3

Th-CTL Peptide Prototype Vaccine Immunogens for Testing in Either Mice, Rhesus Macaque or Human

Vaccine number	Name of Peptides	Species in which to be studied	Amino acid sequence	Restricting elements for CTL epitope
1.	Mouse HIV-1 Th-CTL epitopes		Th - CTL	
	A-Th/A-CTL	Mouse	HAGP ² IAPGQNR ⁴ REPRG-KQI ⁵ IN ⁶ QEVGKAMYA	H- ²
	B-Th/B-CTL	Mouse	KEKVYLA ² WVPAHKGIG-NYAPP ⁶ IGGQI	H-2 K ⁴
	C-Th/C-CTL	Mouse	QLL ² THFRIGCRH ⁵ SR-DRV ⁶ IEVQGAYRAIR	H-2 ¹ (D ¹)
	D-Th/D-CTL	Mouse	EQM ² HEDITISLWDQSL-RIHIC ⁶ G ⁷ RAFYT ⁸ KN	H-2 D ⁴
3.	Macaque SIV/HIV-1 Th-CTL epitopes		Th - CTL	
	Th1/CTL/SIV Gag	Macaque	ELY ² KVVKV ⁴ I ⁵ EPLGV ⁷ APTKA-CTPYDINCM	Maca-A*01
	Th2/CTL/SIV Pol	Macaque	VST ² VCTH ⁴ G ⁵ IRPVV ⁷ STQLL- ⁸ STPP ⁹ L ¹⁰ RL	Maca-A*01
	Th3/CTL/HIV-1 Env	Macaque	STS ² IRGKV ⁴ KEYAFFYKLDI-YAPP ⁷ ISGQI	Maca-A*01
5.	Macaque SIV/HIV-1 Th-CTL p11c epitope variants		Th - CTL	
	Th1/CTL/SIV Gag	Macaque	ELY ² KVVKV ⁴ I ⁵ EPLGV ⁷ APTKA-CTPYDINCM	Maca-A*01
	Th2/CTL/SIV Gag/p11c-Y	Macaque	VST ² VCTH ⁴ G ⁵ IRPVV ⁷ STQLL- ⁸ CTPYDYNQML	Maca-A*01
	Th3/CTL/SIV Gag/p11c-A	Macaque	STS ² IRGKV ⁴ KEYAFFYKLDI- ⁷ CTPYDANQML	Maca-A*01
	Th4/CTL/SIV Gag/p11c-D	Macaque	EYAFFYKLDI ⁷ IP ⁸ NDT ⁹ T ¹⁰ Y- ¹¹ CTPYDDNQML	Maca-A*01
	Th5/CTL/SIV Gag/p11c-K	Macaque	REQFGNNK ² T ³ IPKQSSGGDPE- ⁶ CTPYDKNQML	Maca-A*01
6.	Human HIV-1 Th-CTL overlapping epitopes		Th - CTL	
	A-Th/A-CTL	Human	KQI ² INMW ⁴ QEVGKAMYA-KAFSPEV ⁷ IPMF	HLA B57,B53
	B-Th/B-CTL	Human	YKR ² WIL ⁴ GLNK ⁶ I ⁷ VRMYS-NPP ⁸ IPVG ¹⁰ Y ¹¹ ERW ¹² I- ¹³ ELGLN ¹⁴ K ¹⁵ I ¹⁶ Y ¹⁷ MSPTSI	HLA B35,B8,B37,A33,Bw62,B52
	C-Th/C-CTL	Human	DRV ² IEV ⁴ VQGAYRAIR-WGFP ⁷ VRPQV ⁹ PLR ¹⁰ W ¹¹ YK	HLA A1,B7,B8,B35,A11,A2,A3,A31
	D-Th/D-CTL	Human	ASLWNWFNIT ⁴ INW ⁵ LY-WY ⁶ Y ⁷ TQ ⁸ FFP ⁹ WQ ¹⁰ NY ¹¹ P	HLA B7,B57,A1,B8,B13,B35
8.	Human HIV-1 Th-dominant/ subdominant CTL epitopes		Th - CTL	
	A-Th/E-CTL	Human	KQI ² INMW ⁴ QEVGKAMYA-SILENTVATL	HLA A2
	B-Th/F-CTL	Human	YKR ² WIL ⁴ GLNK ⁶ I ⁷ VRMYS-KIRLRPGGK	HLA A3
	C-Th/G-CTL	Human	DRV ² IEV ⁴ VQGAYRAIR-KR ⁶ W ⁷ ILGLNK	HLA B27
	D-Th/H-CTL	Human	ASLWNWFNIT ⁴ INW ⁵ LY- ⁶ GGK ⁷ AY ⁸ YL	HLA B8
	E-Th/I-CTL	Human	MRE ² PRGSK ⁴ IAGTT ⁶ ST- ⁷ ERY ⁸ LDQQL	HLA B14
10.	Human HIV-1 Th-CTL p17 epitope (A2 Variants)		Th - CTL	
	B-Th/E-CTL	Human	YKR ² WIL ⁴ GLNK ⁶ I ⁷ VRMYS-SILENTVATL	HLA A2
	C-Th/J-CTL	Human	DRV ² IEV ⁴ VQGAYRAIR-SLFNT ⁷ VATL	HLA A2
	A-Th/K-CTL	Human	QI ² INMW ⁴ QEVGKAMYA-SLYNTVATL	HLA A2
	D-Th/L-CTL	Human	ASLWNWFNIT ⁴ INW ⁵ LY-SLYNT ⁷ VATL	HLA A2
	E-Th/M-CTL	Human	MRE ² PRGSK ⁴ IAGTT ⁶ ST-SLFNT ⁸ VATL	HLA A2

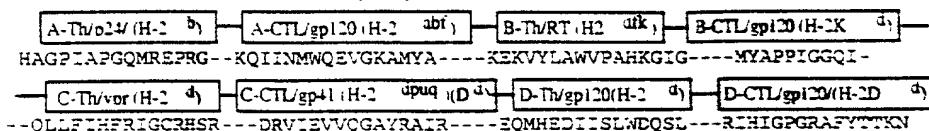
Vaccine number	Name of Peptides	Amino acid sequence	Restricting elements for CTL epitope
11.	Human HIV-1 Th-CTL overlapping epitopes	Th - CTL	
	A*-Th/J-CTL	KQI ² INMWQVVGKAMYA-GQM ⁴ VHQ ⁵ AIS ⁶ P ⁷ R ⁸ T ⁹ L ¹⁰ N ¹¹ A ¹² W ¹³ V ¹⁴ K ¹⁵ V	A2, A202,A5, B7, B14, B57, B5701, B5801, B02, Cw3
	A*-Th/K-CTL	KQI ² INMWQVVGKAMYA-ATPQDLNTMLNTVG ⁶ GHQAAMQMLKETINE ¹⁰ EEAAEW	A2,A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102
	A*-Th/L-CTL	KQI ² INMWQVVGKAMYA-GPKEP ⁴ FRDYVDR ⁶ FYK ⁷ TLRAE ⁸ QAS ⁹ QEV ¹⁰ KNWMT	A2,A202,A5,A24,A2402,A25,A26, A33, B7, B8,B12, B14 B35,B39, B44, B52, B53Bw62, B27, B2705, B57, B5701, B70, B71,Bw62, Cw3, Cw8, Cw0401
	A*-Th/M-CTL	KQI ² INMWQVVGKAMYA- ⁴ KIRLRPGKK ⁷ Y ⁸ KLKHIV ¹⁰ W ¹¹ G ¹² SEELR ¹³ S ¹⁴ LYNT ¹⁵ VATL ¹⁶ YCVHQRI	A1,A2,A3, A3.1,A03, A11, A23, A24, A0201, A2402, B8, B27, B42, B62, Bw62, Cw4

A*-Th=C4E9V

Table 4

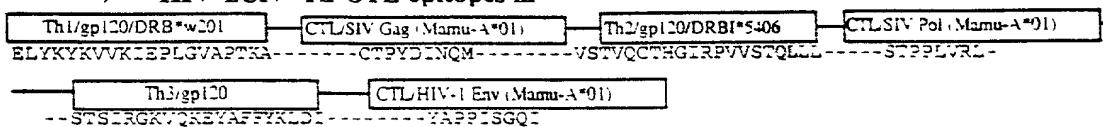
Linear Array of Th-CTL Epitopes To Be Expressed in Modified Vaccinia Ankara

MVA-1) HIV-1 mouse Th-CTL epitopes in



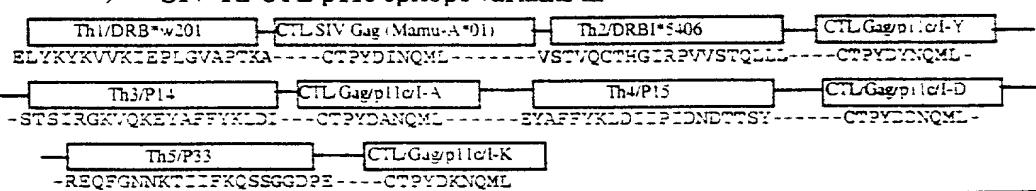
MVA-2) p55/gag + the same HIV-1 mouse Th-CTL epitopes in MVA-1

MVA-3) HIV-1/SIV Th-CTL epitopes in

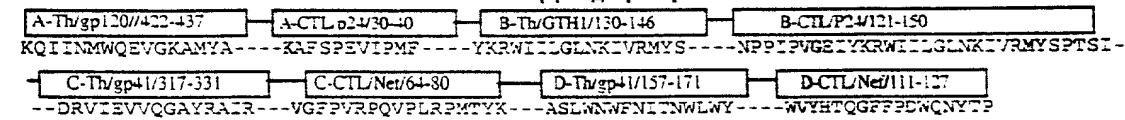


MVA-4) p55/gag + the same HIV-1/SIV Th-CTL epitopes in MVA-3

MVA-5) SIV Th-CTL p11c epitope variants in



MVA-6) HIV-1 human Th-CTL overlapping epitopes in



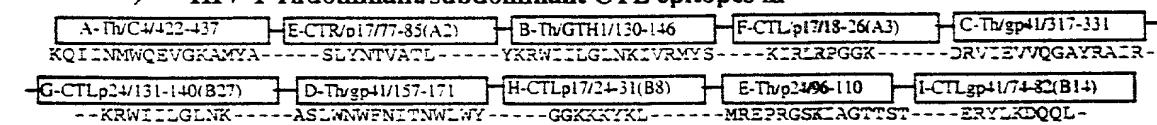
Restricting elements for CTL epitopes:

A-CTL epitope=HLA B57/B58; B-CTL epitope=HLA B35/B8/B27/A33/Bw62/B52;

C-CTL epitope=HLA A1/B7/B8/B35/A11/A2/A3/A31; D-CTL epitope=HLA B7/B57/A1/B8/B13/B35.

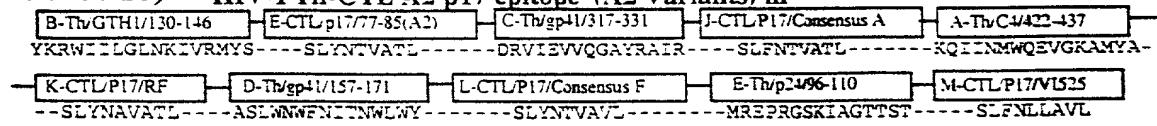
MVA-7) p55 gag +the same HIV-1 human Th-CTL overlapping epitopes in MVA-6

MVA-8) HIV-1 Thdominant/subdominant CTL epitopes in



MVA-9) p55/gag + the same HIV-1 Th-dominant/subdominant CTL epitopes in MVA-8

MVA-10) HIV-1 Th-CTL A2 p17 epitope (A2 Variants) in



Tables 5

HIV Polyvalent C4-V3 Peptides Studied in Guinea Pigs, Primates Or In Humans

Peptide	gp120 C4 Region	gp120 V3 Region
C4-V3MN	KQIINMWQEVGKAMYATRPNPKRRIHIGPGRAFYTTK	
C4-V3RF	KQIINMWQEVGKAMYATRPNNNTRKSITKGPGRVIVATG	
C4-V3EV91	KQIINMWQEVGKAMYATRPGNNTRKSIPIGPGRAFIATS	
C4-V3CanOA	KQIINMWQEVGKAMYATRPHNNTRKSIHMGPGKAFYTTG	
C4E9G-V3RF	KQIINMWQGVGKAMYATRPNNNTRKSITKGPGRVIVATG	
C4E9V-V3RF	KQIINMWQVVGKAMYATRPNNNTRKSITKGPGRVIVATG	
C4K12E-V3RF	KQIINMWQEVGEAMYATRPNNNTRKSITKGPGRVIVATG	
Sequences from the Los Alamos Database.		

TABLE 6

Th-CTL Peptide Prototype Vaccine Immunogens derived from HIV-1 gag

Vaccine number	Name of Peptides	Amino acid sequence	Restricting elements for CTL epitope
	Human HIV-1 Th-CTL overlapping epitopes	Th CTL	
6	A-Th/A-CTL	KQIINMWQEVGKAMYA-KAFSPEVIPMF	B57,B58
6	B-Th/B-CTL	YKRWIILGLNKIVRMYS-NPPPIPVGELYKRWIILGLNKIVRMYSPTSI	B35,B8,B27,A33,Bw62,B52
11	A*-Th/J-CTL	KQIINMWQVVGKAMYA-GQMVHQAIISPRTLNNAWVKVV	A2, A202,A5, B7, B14, B57, B5701, B5801, B02, Cw3
11	A*-Th/K-CTL	KQIINMWQVVGKAMYA-ATPQDLNTMLNTVGGHQAAMQMLKETINEEEAAEW	A2,A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102
11	A*-Th/L-CTL	KQIINMWQVVGKAMYA-GPKEPFRDYVDRFYKTLRAEQASQEVKNWMT	A2,A202,A5,A24,A2402,A25,A26, A33, B7, B8,B12, B14 B35,B39, B44, B52, B53Bw62, B27, B2705, B57, B5701, B70, B71.Bw62, Cw3, Cw8, Cw0401
11	A*-Th/M-CTL	KQIINMWQVVGKAMYA-KIRLRPGGKKKYKLLKHTIVWGSEELRSLYNTVATLYCVHQRI	A1,A2,A3, A3.1,A03, A11, A23, A24, A0201, A2402, B8, B27, B42, B62, Bw62, Cw4

A*-Th=C4E9V

Summary of restricting elements for CTL epitopes in Vaccines A, B, J, K, L and M

A: A1, A2 (02), (01), A3, A3.1, A5, A11, A23, A24 (02), A25, A26 and A33.

B: B7, B8, B12, B14 (02), B27 (05), B35, B39, B42, B44, B52, B53, B57 (01), B58 (01) B62 (w62), B70 and B71.

C: Cw3, Cw4, Cw0401 and Cw8.

HIV Th/CTL vaccine ABJKLM